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Accuracy of transthoracic ultrasonography in diagnosis of post procedure pneumothorax.

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Accuracy of transthoracic ultrasonography in diagnosis of post procedure pneumothorax

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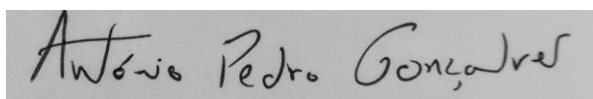
Orientador – António Pedro Esteves da Gama Gonçalves

Co-Orientador – Professora Doutora Evren Üstüner


Maio de 2018

A handwritten signature in black ink, reading "Ana Soares Jorge". The signature is fluid and cursive, with the first name "Ana" being more prominent.

Ana Soares Jorge

A handwritten signature in black ink, reading "António Pedro Gonçalves". The signature is written on a light gray rectangular background and is in a cursive style.

António Pedro Esteves da Gama Gonçalves

A handwritten signature in blue ink, reading "Evren Üstüner". The signature is written on a white background with a horizontal line above and below it, and is in a cursive style.

Evren Üstüner

Ankara, 31 de maio de 2018

Dedicatória

Para ti Mãe.

“ Se alguém ama uma flor da qual só existe um exemplar em milhões e milhões de estrelas, isso basta para fazê-lo feliz quando as contempla.
Ele pensa: Minha flor está lá, em algum lugar... Mas se o carneiro come a flor, é, para ele, como se todas as estrelas se repentinamente se apagassem!
E isto não tem importância?”

Antoine de Saint-Exupéry, O pequeno Príncipe

Agradecimentos

O que inicialmente parecia ser fácil, ganhou novo significado agora, à conclusão deste percurso. À minha casa, o Instituto de Ciências Biomédicas Abel Salazar, que fez mais do que o seu papel enquanto instituição académica, mas me fez crescer e aprender a ser humana e médica.

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Resumo

Introdução: O pneumotórax é um problema frequente nos serviços de emergência e cuidados intensivos, podendo ocorrer espontaneamente, após trauma, ou como complicação de procedimentos como toracocentese e biópsia pulmonar. O método de diagnóstico gold standard é a imagem radiológica, incluindo a tomografia computadorizada e a radiografia do tórax. Para além dos efeitos da radiação, estas modalidades não podem ser realizadas à cabeceira do paciente. A ultrassonografia point-of-care (POCUS) está a tornar-se uma parte integral da prática clínica, podendo ser realizada rapidamente e facilmente.

Objetivo: O nosso objetivo foi analisar os dados obtidos a partir da literatura disponível, avaliando a acuidade da ultrassonografia torácica no diagnóstico do pneumotórax após procedimentos torácicos invasivos. O nosso segundo objetivo foi propor uma metodologia para o diagnóstico de pneumotórax iatrogénico, a ser aplicada neste contexto e no futuro, incluída em um estudo que poderá fortalecer os resultados obtidos por outros autores.

Métodos: Em maio de 2018, realizámos uma revisão da literatura de artigos de pesquisa publicados em inglês, entre janeiro de 1995 e março de 2018 no Medline e EMBASE, avaliando as características de teste da ultrassonografia em comparação com a radiografia torácica após intervenção. Artigos elegíveis foram definidos como estudos em pacientes submetidos a procedimentos torácicos e submetidos a investigação diagnóstica de pneumotórax com ultrassonografia e radiografia torácica. Os dados extraídos foram analisados, sendo calculados a sensibilidade, especificidade e o diagnostic *odds-ratio* global da ultrassonografia, utilizando o software freeware Meta-DiSc, versão 1.4.

Resultados: Oito artigos foram considerados adequados para a análise estatística, compreendendo um total de 1.123 pacientes. A ultrassonografia mostrou uma sensibilidade de 89,7% (95% CI, 82,8 - 94,6) e especificidade de 97,9% (95% CI, 96,8-98,7) para a detecção do pneumotórax pós-procedimento. A radiografia de tórax apresentou uma sensibilidade de 48,6% (95% CI, 38.8-58.5) e uma especificidade de 99,3% (95% CI, 98.2-99.8). O diagnostic *odds-ratio* obtido para ultrassonografia e radiografia torácica foi 397.80 (95% CI, 79.204-1998.0), e 113.52 (95% CI, 15.378 to 837.96) respetivamente.

Conclusão: A ultrassonografia é mais sensível e pelo menos tão específica como

a radiografia do tórax. Possivelmente, pode substituí-la no diagnóstico e exclusão do pneumotórax iatrogénico. A radiografia pode ser apenas necessária quando a qualidade do estudo ultrassonográfico não é considerada adequada.

Palavras-chave: Pneumotórax, pós-procedimento, ultrassonografia.

Abstract

Background: Pneumothorax (PNX) is a frequent problem in the emergency and critically care settings, and can occur spontaneously, due to trauma, or as complication of interventional procedures as thoracentesis, and lung biopsy. The gold standard in the diagnosis of PNX is radiographic imaging including computerized tomography (CT) and chest radiography (CR). Beside the effects of the irradiation, CT and CR cannot be performed at the bedside of the patient. Thus, Point-of-care ultrasonography (POCUS) is becoming an integral part of the clinical practice, being quickly and easily performed.

Purpose: We aimed to analyse the data gained from the available literature evaluating the accuracy of thoracic ultrasound in the diagnosis of post-procedure PNX. Our second goal was to propose a methodology for the diagnosis of pneumothorax, that could be applied in a post-interventional setting, and in the future included in a study that could support the findings reported by previous studies.

Methods: In May 2018, we performed a literature review of published research articles in English, between January 1995 and March 2018 in Medline and EMBASE, evaluating the test characteristics of US in comparison with CR at a post-interventional setting. Eligible articles were defined as studies on patients submitted to thoracic procedures who underwent PNX screening with chest US and CR. The data extracted were analysed and pooled sensitivity, specificity and diagnostic odd ratio of US calculated with freeware Meta-DiSc, version 1.4 software.

Results: Eight articles were found suitable for the statistical analysis, comprising a total of 1,123 patients. Overall, ultrasonography was 89.7% sensitive (95% CI, 82.8-94.6) and 97.9% specific (95% CI, 96.8-98.7) for the detection of post-procedure PNX. Chest radiography had a pooled sensitivity of 48.6% (95% CI, 38.8-58.5) and a specificity of 99.3% (95% CI, 98.2-99.8). The pooled DOR for US was 397.80

(95% CI, 79.204 to 1998.0), whereas for CR, the pooled DOR was 113.52 (95% CI, 15.378 to 837.96).

Conclusion: Although the gold standard diagnosis modality of pneumothorax is still computerized tomography, ultrasonography is more sensitive and at least as specific as CR, and possibly can substitute CR in diagnosis and exclusion of iatrogenic pneumothorax. CR may only be needed, when the quality of sonography findings is poor.

Key Words: Pneumothorax, post procedure, ultrasonography.

Abbreviations

BLUE	Bedside lung ultrasound in emergency
CR	Chest radiography
CT	Chest tomography
e-FAST	extended FAST
FAST	Focused assessment with sonography for trauma
PNX	Pneumothorax
POCUS	Point-of-care ultrasonography
TBLB	Transbronchial lung biopsy
TNAB	Transthoracic needle aspiration and biopsy
US	Ultrasonography

Index

Resumo	ii
Abstract	iii
Tables Index	vii
Figures Index	viii
Introduction	1
Material and Methods	2
<i>Studies inclusion criteria</i>	3
<i>Data extraction and management</i>	3
Methodology for a future prospective study	3
<i>Patient Eligibility</i>	3
<i>Study design</i>	4
<i>Lung Ultrasound Examination</i>	4
Results	5
Discussion	5
Conclusion	9
APPENDIX I.....	10
APPENDIX II.....	11
APPENDIX III.....	12
APPENDIX IV	13
APPENDIX V	14
References	15

Tables Index

Table I Characteristics of included studies	11
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Figures Index

Figure 1 Decision tree of the BLUE protocol	10
Figure 2 Areas of US investigation and the BLUE-points	12
Figure 3 Forest plot for sensitivity, specificity of US	14
Figure 4 Forest plot for sensitivity, specificity of CR	14
Figure 5 Forest plot for diagnostic odds ratio of US and CR	14

Introduction

Pneumothorax (PNX) is frequently seen in emergency and critical care settings with significant morbidity and mortality rates. It can occur spontaneously, as a result of trauma or as a complication of various procedures, such as thoracentesis and lung biopsy.¹ Deferred diagnosis or treatment can lead to hemodynamic or respiratory compromise.¹⁻³ Thus, early diagnosis is important for prognosis. The diagnosis of PNX starts with suspicion according to the clinical findings³ and is confirmed by imaging. The gold standard diagnosis modality of PNX is computerized tomography (CT) of the chest but it has major drawbacks such as the necessity of patient transfer, delay in the diagnosis during transfer, irradiation, and cost.⁴ Chest radiography (CR) is commonly the first imaging method in daily practice⁵ although it has been demonstrated to be an insensitive and unreliable test in the diagnosis of limited PNX² with misdiagnosis rates between 30% and 40%.⁴ Therefore there is increasing interest in alternative techniques, that can be immediately implemented at bedside and accurately exclude pneumothorax.⁴

Point-of-care ultrasonography (POCUS) is now an integral part of the clinical practice, mainly in emergency and critical care but also has other diagnostic and procedural applications.^{6,7} It is a focused examination defined as bedside ultrasonography that allows immediate and repeated assessments of the patient using real-time dynamic images, directly correlated with the patient's signs and symptoms.⁷ Through the identification of major signs that yield specific and standard profiles^{8,9} POCUS allows to safely and efficiently diagnose or rule out conditions presented as hypotension, chest pain, or dyspnoea, reconsider priorities by the use of life-saving protocols^{7,9} (BLUE-protocol, Figure 1 - *Appendix I*), reduce the need for CT or other diagnostic procedures (as diagnostic laparotomy or arterial blood gas) and reduce the time to appropriate intervention, resulting in a shorter hospital stay, lower costs and overall mortality.⁷

Ultrasonography (US) of the chest, was previously limited to the study of pleural effusion and superficial thoracic masses.¹⁰ Recently, it has been highlighted that the lung is highly sensitive to variations of the pulmonary content and balance between air and fluids.¹¹ As aeration of lung tissue is reduced, interstitial and alveolar fluids increase or when air and fluids are collected in the pleural space, visual assessment of several pathologic entities becomes possible by the identification of characteristic artefacts, that differ from the healthy lung.¹¹⁻¹³

The dynamic and static analysis of a combination of these artefacts has a high diagnostic accuracy for common thoracic conditions, especially for pleural and parenchymal abnormalities.⁶

Considering the impact of lung US in the assessment of respiratory and hemodynamic status of the patient, the integration of the technique in different settings is essential and indeed can be done easily without complex adaptation being cost-effective.⁸

Several early trials showed a strong superiority in favor of US over CR,¹⁴ and US may be a better diagnostic strategy as an initial diagnostic study in critically ill patients with suspected pneumothorax.¹⁵ Despite those and other accumulating original research evidence favoring ultrasonography, US remained underused due to the ready availability of CR.¹⁴

Experience with ultrasonography in the identification of iatrogenic pneumothorax is limited.¹⁶ In the few reports published, a small number of patients were enrolled and conflicting results were obtained.¹⁷ So, there is the need of further studies that can validate the superiority of lung ultrasound, not only in ruling out post interventional complications as pneumothorax but also confirm enhanced health outcomes.⁶

We aimed to conduct a review of the literature evaluating the accuracy of thoracic ultrasonography in the detection of post procedure pneumothorax, and calculate the pooled test characteristics, with the data extracted. Based on the literature available and considering the need of larger prospective studies to validate the utility of US in this field, we planned and present a methodology of a future study that aims to support the findings in previous studies.

Material and Methods

We performed a literature review of published research articles evaluating the diagnostic accuracy of US in comparison with CR at a post-interventional setting. No institutional review board approval or consents were needed, as it evaluated published studies without individually identifiable human subjects information.

We searched original articles published in English language from 1995 up to march 2018 in Medline and EMBASE. Our initial search was broad and included subject headings, truncated terms, and text words: “ultrasound” or “sonography” and “ultrasonography” or “radiography” or “chest film” or “chest radiograph” and “CT” or “chest tomography”, “pneumothorax”, and “iatrogenic” or “post procedure” or “post interventional”.

References of the initially chosen articles were also subjected to a secondary hand search, and relevant articles were extracted. No attempt was made to include unpublished data.

Studies inclusion criteria

The inclusion criteria used to select the articles are as follows:

- (a) Prospective studies that evaluate the diagnostic performance of ultrasonography, CR, or both for the detection of procedure related PNx;
- (b) Comparison of US imaging results with CR or gold standard (CT scan);
- (c) Description of diagnostic criteria for pneumothorax on US in clear details;

Exclusion criteria were:

- (a) Differential verification methods (two different reference standards);
- (b) Long waiting time (defined as more than 6 hours) between index test and reference standard or vice versa;
- (c) Insufficient details of the execution of the index test or the reference standard;
- (d) Lack of either CT-scan or CXR verification or US arm.
- (e) Studies that included populations with known pneumothorax.

Data extraction and management

We completed our initial search strategy in march 2018. One of the authors independently reviewed the articles based on manuscript titles and abstracts, and extracted data. The data were analyzed with freeware Meta-DiSc, version 1.4 software. To explain the observed heterogeneity within studies, a random-effect model was used to calculate pooled sensitivity and specificity and Diagnostic odds ratio (DOR) with corresponding 95% confidence intervals (CI). Statistical heterogeneity was measured using the Chi^2 tests ($p < 0.10$ was representative of significant statistical heterogeneity)¹⁸, and inconsistency index (I^2). Possible causes of the variation observed were not explored.

Methodology for a future prospective study

Patient Eligibility

We propose to include patients with 18 years or older undergoing CT or US guided transthoracic biopsy. Patients will be excluded if they (a) develop an intraoperative pneumothorax, (b) declined to provide informed consent, (c) decline to undergo an ultrasound examination or CR, (d) have a preexisting pneumothorax, (e) have a chest drain in situ or other objects that would make ultrasound examination difficult, (f) if they do not undergo biopsy. Written informed consent will be obtained from enrolled participants. The local Ethics Committee must grant a previous approval to the study.

Study design

Patients will undergo a preprocedure lung ultrasound, to identify any preexisting anatomic variants, pneumothorax, lung pathology, and for comparison with postprocedure images. Intraoperatively and immediately postbiopsy, patients will be examined for pneumothorax – with chest CT or US, according to the biopsy method. Thoracic ultrasonography will be performed within 60 minutes after transthoracic biopsy. As per institutional protocol, a CR will be done to all patients until 2 hour after biopsy to assess for pneumothorax. The CR findings will be reported by a consultant radiologist blinded to the study protocol and the patient's clinical status. Because of the additional radiation exposure, CT examination of the chest is not planned to be performed routinely, but only in case of disagreement between US and CR findings. Concordance between the results of transthoracic sonography and chest radiography will be considered sufficient for diagnosis or exclusion of pneumothorax. When diagnosed, complications will be treated according to international recommendations and sonographically monitored.

Lung Ultrasound Examination

All sonographic examinations will be performed by a 6th year medical student that previously attended to an 80 hours ultrasound training workshop and underwent an initial training period of 1 week. An experienced radiologist in chest sonography will confirm the findings. Both operators will be blind to CR/CT scan results to eliminate any bias in the study.

The scanning technique planned is adapted from the emergency setting – BLUE points (Figure 2 - *Appendix III*; Lichtenstein, 2017).⁹ The images will be obtained in a longitudinal scanning plane with the transducer indicator in a sagittal position along standardized thoracic points, starting from the biopsy site. Posterior thoracic wall will be also examined, considering the biopsys realized in that localization. The pleural surface will be identified as a hyperechoic line between 2 ribs shadows.

Pneumothorax will be diagnosed by a sequential approach, that involved the identification of 4 signs, according to recent recommendations by an expert panel¹⁵ and the BLUE protocol (Figure 1- *Appendix I*; Lichtenstein, 2017)⁹: (1) recognise the A'-profile; (2) find the lung point extending from the area with the A'-profile, laterally until the appearance of lung sliding and B-lines. If the lung point sign is absent, (3) identify the lung pulse (the lung pulse excludes a pneumothorax)¹⁹. If pneumothorax is suspected, M-mode images will be obtained as an adjunct. Additional information about

ultrasonography based diagnosis of PNx can be found in *Appendix IV*.

Results

We found 8 articles that met all the inclusion criteria and were considered eligible for a statistics analysis (Table I - *Appendix II*). The studies involved a total of 1,123 patients that underwent to invasive thoracic procedures as CT-guided lung biopsy (289 patients), transbronchial lung biopsy (379 patients), transthoracic needle aspiration and biopsy of the lung (TNAB) (97 patients), transthoracic sonographically guided lung biopsy (285 patients), thoracentesis (78 patients) and CT-guided cryoablation of a lung mass (1 patient).

Three of the studies^{4,16,20} did not report chest radiograph data. Therefore, chest radiograph data were available for 660 of the 1,123 patients. One study¹⁷ didn't report clearly the number of patients in whom pneumothorax was diagnosed or excluded by US, and so was not included in US test characteristics analysis.

Chest radiographs were performed in the semierect position in 34 patients, in supine position in 247 patients, and in the erect position in 876 patients.

Overall, ultrasonography was 89.7% sensitive (95% CI, 82.8 – 94.6) and 97.9% specific (95% CI, 96.8-98.7) (Figure 3 – *Appendix V*). In comparison, chest radiography had a pooled sensitivity of 48.6% (95% CI, 38.8-58.5), a specificity of 99.3% (95% CI, 98.2-99.8) (Figure 4 – *Appendix V*). The pooled DOR for US was 397.80 (95% CI, 79.204 to 1998.0), whereas for CR, the pooled DOR was 113.52 (95% CI, 15.378 to 837.96) (Figure 5 – *Appendix V*).

The significant Ch^2 values, shown in the forest plots for each test, implied that there were causes of heterogeneity other than a cutoff effect. The possible source of heterogeneity in US and CR findings were not studied in our analysis.

Discussion

The statistical analysis of the reviewed articles demonstrates significantly superior pooled sensitivity, odds of accurate diagnosis and similar pooled specificity in the use of ultrasonography compared with CR for the diagnosis of PNx.

Previous meta-analyses, studied and compared the test characteristics of US in the diagnosis of PNx within studies, in different settings (trauma, and non-trauma), but few articles related to diagnosis of post-procedure PNx by US, were included.^{1,2,14,21}

The pooled specificity in our analysis (97.9%) is similar to the results reported by Ding et al.², Alrajhi et al.¹, Ebrahimi et al.²¹ and Alrajab et al.¹⁴ (99%, 98.2%, 99% and 98.4%

respectively). With the exception of one study, that reported a pooled sensitivity for US of 78.6%¹⁴, our result (89,7%) is also comparable with the results obtained by other authors (88%², 90.9.%¹, 87%²¹). The value of DOR reported by the previous analysis, is also in the same line of our results (397.80 versus 279.3¹⁴, 465.52²¹ with the exception of the results obtain by Ding et al.² (993.52).

Our results, revealed a high degree of heterogeneity within studies. Possible sources were considered but not analysed as in previous studies: operator, ultrasound probe used, ultrasonographic signs used as criteria to diagnose PNx.^{1,2,14,21} The operator, differences between their skill, experience, knowledge of chest ultrasonography, and the type of subject (trauma/non trauma settings) were considered to be the main causes of this heterogeneity within studies.^{2,21} Recent meta-analysis revealed the pooled sensitivity and specificity of US performed by nonradiologist physicians to be 89% and 99%, respectively.² In Alrajab et al.¹⁴ emergency physicians performed better US than nonemergency physicians, with a sensitivity of 82.3% and 72.8% respectively, possibly because their experience with chest US, now included in the eFAST (Extended Focused Assessment with Sonography for Trauma)²¹. However, this fact does not underestimate the value of US, or limit its use in other settings. Studies show the learning curve for sonographic pneumothorax detection is short and steep¹⁶ and can be accurately performed by operators with no prior ultrasound experience after 2 hours of training.^{22,16} Although still performing better than chest radiography, ultrasonography sensitivity was low in 3^{3,16,20} of the included studies for comparison.

Kumar et al.⁽⁴⁾ investigated the utility of bedside ultrasound for diagnosis of post-TBLB pneumothorax. In their study the sensitivity, specificity, PPV, and NPV of US was 100%. Similarly Bensted et al.²⁰ reviewed the use of ultrasound in screening for pneumothorax following TBLB in post-lung transplant patients. The sensitivity and specificity of ultrasound was 75% and 93%, respectively, with a PPV of 35% and a NPV of 99%. In this study, the operator was not specifically trained in lung ultrasound, and an ultraportable handheld ultrasound device was used which could have affected the interpretation of the ultrasonography findings.²⁰ Other important consideration was the conservative approach of the operator, in the screening of patients with already compromised lung function and limited quality US findings, thereby over diagnosing PNx and lowering PPV.²⁰

In 2013, a meta-analysis¹⁴ assessed the efficacy of sonography in detecting PNx, only including studies that compared ultrasound and CR with CT. In Chung et al.³, CT scans were also performed in all the patients. Their finding of a lower sensitivity on ultrasonography examination may be explained by the fact that CT was detecting small, subclinical pneumothoraces not seen by ultrasound or CR.¹⁴ In the majority of studies

discussed, CT was not routinely performed postprocedure. Therefore, the true prevalence of occult pneumothoraces is unknown and the diagnostic accuracy of transthoracic sonography may have been overestimated.

Previous studies underlined the fact that lung sliding may be absent or difficult to recognise in cases of bullous emphysema, paralysis of the phrenic nerve and pachypleuritis, thereby leading to false positive diagnoses when absent lung sliding is considered sufficient for the diagnosis.^{23,16} Moreover this sign can be difficult to appreciate in the upper chest quadrants in healthy patients as well.²³ Volpicelli¹⁹, reported high values of sensitivity (100%), PPV (100%) and specificity (96.5%) with use of the simultaneous absence of lung sliding and B-lines as a criterion to exclude pneumothorax. In the articles reviewed, the M-mode^{4,13} and power Doppler²⁴ were used as adjuncts on the diagnosis of PNx, but the signs accessed by these (Seashore sign and power slide sign) are different graphical displays of lung sliding, being unlikely to affect significantly the test characteristics.¹ The data available about the use of this additional methods, are also not enough to analyse the individual performance of the US signs detected by them.¹

Some of the studies analyzed included patients with underlying lung disease.^{16,20} Shostak et al.¹⁶ could not obtain an adequate image the pleural surface in 43 of 185 patients (23%). In Bansted et al.²⁰, 3 of the 11 patients (27.3%) who had a false positive diagnosis of pneumothorax demonstrated reduced lung sliding on their preprocedure ultrasound. This could explain the lower specificity and PPV reported in comparison with the other studies.

Slater et al.²⁵ determined the diagnostic accuracy of US in the diagnosis of pneumothorax in patients with COPD. The sensitivity of ultrasonography was 58.9% and specificity, 99.1%. This study concluded that in some patients ultrasonography only can exclude but not confidently diagnose PNx without the use of other imaging modalities.²⁵ So, some authors^{20,16} recommend a pre-procedure ultrasound scan, in order to identify patients in whom a post-procedure ultrasound would not be diagnostic.

Goodman et al.¹⁷ studied the use of ultrasonography on detection of pneumothorax after CT-guided biopsy in 29 patients. In this study the ultrasound examination was limited to the needle entry site, failing to detect six of 13 pneumothoraces.¹⁷ These data suggest that it is insufficient to restrict sonographic examination solely to the needle entry site.²⁴ Although the details of the technique used to perform the ultrasound examination varied within studies, and we did not find any studies comparing them, the majority of the authors agreed that the examination should include the needle entrance point and more than one intercostal space in both hemithoraxes, from the midclavicular line to the midaxillary line,¹ and even if not routinely the posterior axillary line if necessary. It is

possible that this methodology may improve diagnostic accuracy and the exclusion of occult pneumothoraces.¹⁶

The determination of the size of a PNX is important in making procedural and therapeutic decisions.⁴ Even with a limited chest wall examination, US was still found more sensitive at detecting small post-biopsy pneumothoraces than erect chest radiographs.¹⁷ Small pneumothoraces might not require invasive treatment, but are important to recognize, avoiding unnecessary therapeutic procedures.¹⁴ With the dynamic technique of assessing lung points, pneumothorax extension can be derived from the site of lung-point projection with an accuracy almost as high as the reference standard (CT scanning).⁴ Garofalo et al.²³ also reported complete concordance between US and CT findings in quantification of severity of the pneumothorax and confirm the superiority of US over CR, in identification of very small pneumothoraces with a sensitivity of 95.65% and 42% respectively.

Considering some authors³ the supine incidence of CR is less sensitive (37%) than the erect view (59%) in detecting small pneumothorax. Most of the patients included on the analyzed studies had an erect chest radiograph, possibly not underestimating the accuracy of CR. Even considering the possible confounder effect of the patient's position on CR, the sensitivity reported in some studies was only 52%.¹⁴

The lung point is an inconstant, not very sensitive sign (75%),^{8,19} but it is highly specific (100%) even in the identification of radio-occult pneumothorax.^{8,22} An anterior lung point indicates mild or moderate pneumothorax whereas an absent lung point is suspicious for complete pneumothorax, requiring CT to determine the extension.^{4,24} US is still not recognized as the method of choice to differentiate between small and large PNX,¹⁵ with serial CR being recommend¹⁶.

This study has several limitations. We did not attempt to identify unpublished studies, or include articles in other languages, so our analysis included a small number of articles with small sample size and low frequency of post-interventional complications. This may have an effect on the pooled test characteristics obtained and limit the ability to generalize the data.

We noted several advantages of ultrasound over chest radiography. Ultrasonography allows a significantly quicker diagnosis of PNX compared with CR, considering the portability and almost immediate availability of the equipment, after the procedure.^{3,4,13,17,20} US is a relatively easy to learn, dynamic, non-ionizing, less technically demanding tool, independent from specific acoustic windows and therefore suitable for use in different settings.²⁶

If further prospective studies confirm the findings reported, transthoracic sonography should be considered for diagnosing pneumothorax after interventional procedures.¹³

Chest radiography may be reserved for assessment of the extension of pulmonary collapse, if there is discrepancy between sonographic findings and patient's clinical manifestations¹³, limited studies²⁰, or as control after pneumothorax drainage. This approach will reduce ionizing radiation exposure, time delays and costs associated with radiography.²⁰

Conclusion

Fast, reliable pneumothorax detection is vital at the bedside following interventional procedures. Ultrasound does have potential in fulfilling this role. US is a safe and noninvasive method, with high specificity, and so could be use as a screening tool to exclude post-interventional pneumothorax quicker and as accurately as CR.

US is reported to have good interobserver reproducibility when the operators are skilled, however is still an operator dependent test, that requires training and experience.

Larger prospective studies are needed to validate the utility of US not only in diagnosis but also to guide clinicians regarding management of PNX.

APPENDIX I

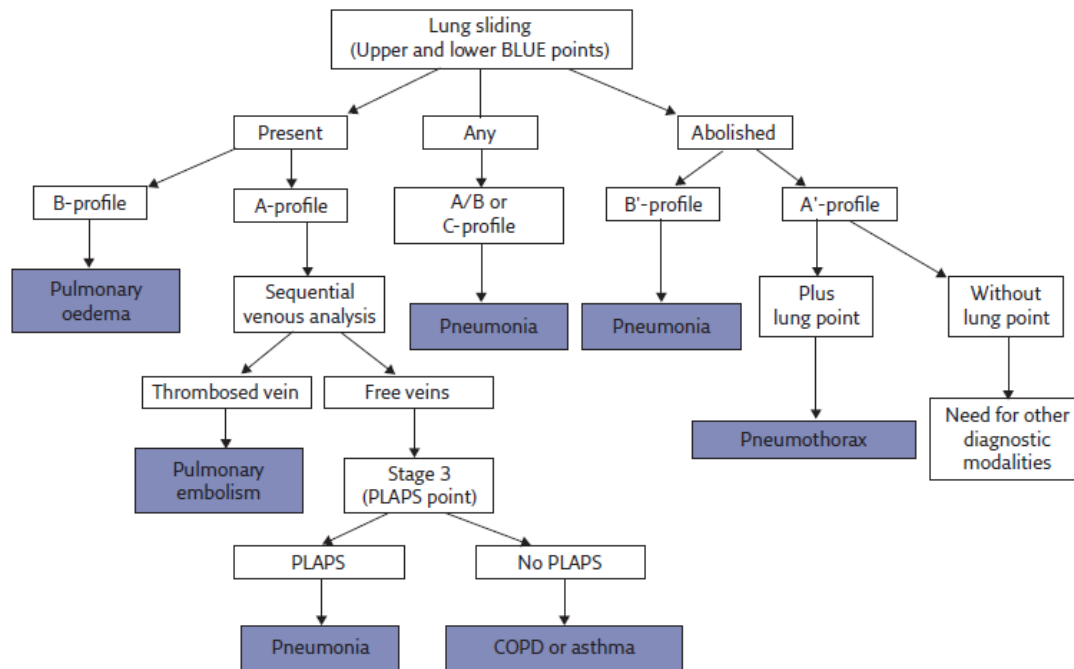


Figure 1 Decision tree of the BLUE protocol. Adapted from Lichtenstein, 2017.⁹

APPENDIX II

Table I Characteristics of included studies; NR not reported, CT comet tail (B-lines), LP lung point, LS lung sliding

Study	Year	Country	Modality	No.	US operator	US signs	US probe
Goodman et al. ¹⁷	1999	United Kingdom	US, CR, CT	41	Radiologist	LS, CT	Linear
Reißig and Kroegel ²⁴	2005	Germany	US, CR	53	Pneumologist	LS, CT, LP	Linear
Chung et al. ³	2005	Korea	US, CR	97	Radiologist	LS, CT	Linear
Garofalo et al. ²³	2006	Italy	US, CR	184	Emergency Physician	LS, CT, LP	Convex
Sartori et al. ¹³	2007	Italy	US, CR	285	NR	LS, CT, LP	Convex
Shostak et al. ¹⁶	2013	United States	US, CR	185	Radiologist/Clinical Investigator	LS, CT	Linear
Kumar et al. ⁴	2015	India	US, CR	113	Clinical Investigator	LS, CT, LP	Linear
Bensted et al. ²⁰	2017	Australia	US, CR	165	Clinical Investigator	LS, CT, LP	Linear

APPENDIX III

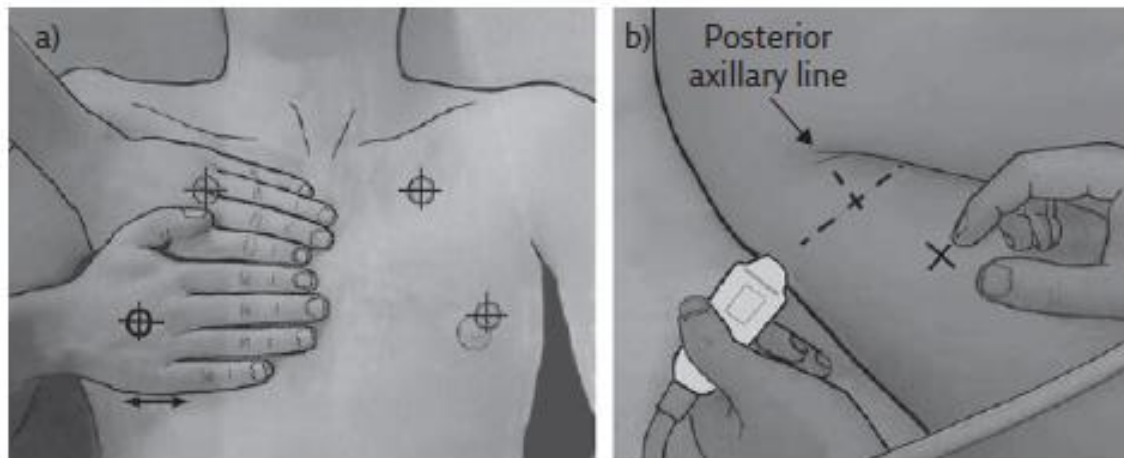


Figure 2 Areas of US investigation and the BLUE-points. Adapted from Lichtenstein, 2017.⁹

The upper BLUE hand is applied parallel and below the clavicle; The lower BLUE hand is applied just below; The upper BLUE point is defined at the middle of the upper BLUE hand. The lower BLUE point is defined at the middle of the palm of the lower BLUE hand.

APPENDIX IV

Lung Ultrasound Examination

The normal lung surface, defined in the BLUE protocol as the A profile (Figure 1-Appendix I), is recognized on US by the presence of lung sliding and horizontal repetitions of the pleural line, called A-lines.⁹ The A'-profile is defined anteriorly in supine patients. It includes abolished lung sliding and the A-line sign (no B-line, should be observed).⁹ This profile is suggestive of pneumothorax, and definite if a lung point is also present.⁹

Lung sliding is the representation of the movement that occurs between the parietal and visceral pleura synchronized with respiration.¹⁵ The B lines appear as vertical lines that originate from the pleural surface, and result from the difference in acoustic impedance between two structures, such as visceral pleura and aerated lung.¹⁶ These artefacts are sporadic in healthy lung and more numerous in diffuse parenchymal disease.¹³ The presence of one or both signs referred previously, imply contact of the visceral pleura with the parietal pleura and can rule out PNx,^{2,15,23} but absence of lung sliding sign or B-lines cannot confirm the existence of PNx.^{2,27} In this setting, a highly specific sign is the lung point, which represents the transition point between the typical sonographic pattern of PNx (absence of lung sliding and B-lines) into the normal pattern of lung sliding, and represent the physical limit of PNx.¹⁵ The lung point is a pathognomonic sign of pneumothorax however must never be sought if no A'-profile has been identified.⁹ The lung pulse refers to the rhythmic movement of the visceral upon the parietal pleura with cardiac oscillations¹⁵ being useful for prompt diagnosis of an atelectasis.⁹ M-mode reveals the seashore sign. Above the pleural line, the motionless chest wall displays a stratified pattern, below the pleural line, the movement of lung sliding show a sandy pattern.⁸ When pneumothorax occurs, the presence of air within the pleural spaces generates reverberation artefacts that form parallel horizontal echoic lines motionless during breathing movements.¹³

In extreme emergency, absence of movement of the pleural line, horizontal (sliding) or vertical (pulse), combined with absence of B-lines, immediate and safely diagnosis pneumothorax without the need for searching the lung point.¹⁵

APPENDIX V

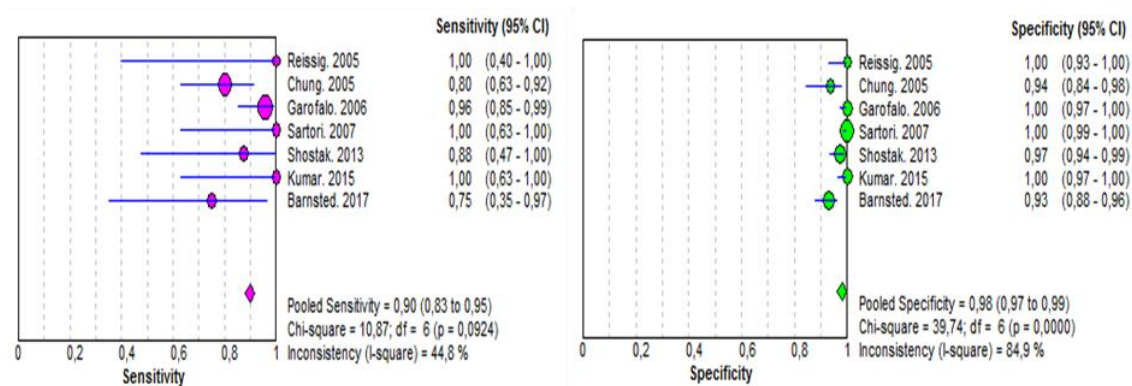


Figure 3 Forest plot for sensitivity, specificity of US for detection of pneumothorax.

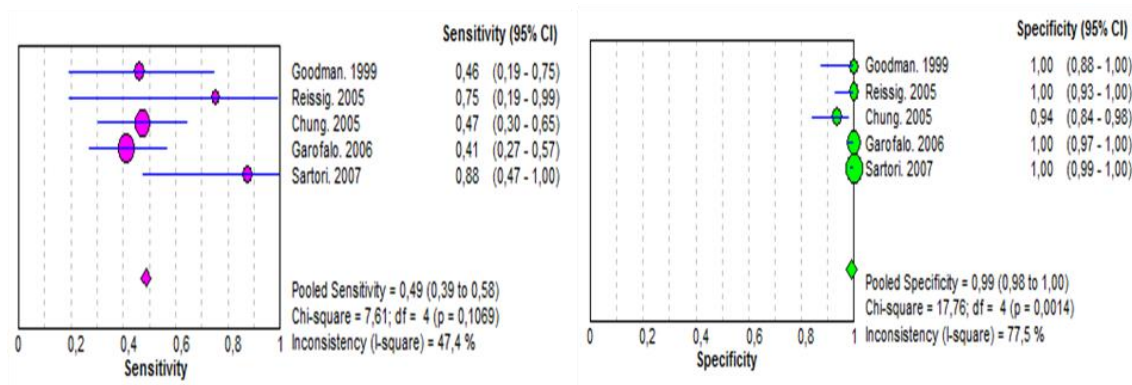


Figure 4 Forest plot for sensitivity, specificity of CR for the detection of pneumothorax.

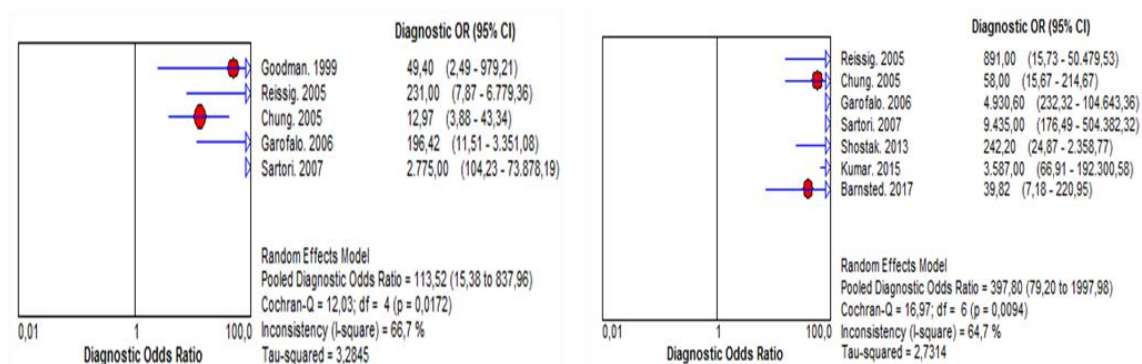


Figure 5 Forest plot for diagnostic odds ratio (DOR) of CR (left) and US (right).

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